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## (54) MANUFACTURE OF FILLER FOR CHROMATOGRAPHY

(57)Abstract:
PROBLEM TO BE SOLVED: To synthesize filler, wherein remaining silanol group is made sufficiently inactive in vapor phase and liquid by chemically bonding chemical modifying agent to the silanol group of silica gel, and making two kinds of end-terminal adding agent forming a partial complex compound to act with the silica gel in the specified temperature range in inactive gas atmosphere.
SOLUTION: After the chemical modifying agent is chemically bonded to the silanol group of silica gel, two kinds of end-terminal adding agents forming partial complex compound is made to react with the silica gel in the vapor phase or the liquid phase of 180-240° C in a tightly sealed container under inactive gas environment atmosphere. An inactivated group is chemically bonded to the remaining silanol group of the silica gel. As the chemical modifying atent, e.g. monochloro silane compound, in details, e.g. dimethyl octadecyl chloro silane or the like is used. In the mepntime, as one end-terminal adding agent, e.g. N-(trimethyl silyl) molpholine is used, and as the other end-terminal adding agent, e.g. trimethyl bromosilane or the like is used.

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## CLAIMS

[Claim(s)]
[Claim 1] The manufacturing method of the bulking agent for chromatographies which at least two sorts of end addition agents which form a complex compound in part at least are made to react with silica gel, and carries out the chemical bond of the deactivating group to the residual silanol group of this silica gel by the 180-240-degree C gaseous phase in the well-closed container under an inert gas ambient atmosphere after carrying out the chemical bond of the chemical modification agent to the silanol group of silica gel.
[Claim 2] The manufacturing method of the bulking agent for chromatographies which at least two sorts of end addition agents which form a complex compound in part at least are made to react with silica gel, and carries out the chemical bond of the deactivating group to the residual silanol group of this silica gel by the 180-240-degree C liquid phase in the well-closed container under an inert gas ambient atmosphere after carrying out the chemical bond of the chemical modification agent to the silanol group of silica gel.
[Claim 3] One end addition agent is the approach according to claim 1 or 2 of choosing from a silazane compound, a disilazane compound, a siloxane compound, and a polysiloxane compound at least one sort.
[Claim 4] The end addition agent of another side is the approach according to claim 1 or 2 of choosing from a halogeno silane compound, an alkylcarbonyloxy silane compound, an alkylsulfonyloxy silane compound, an alkyl borane compound, a dialkylzinc compound, an alkylaluminum compound, an alkyl titanium compound, and an alkyltin compound at least one sort.

[Translation done.]

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## DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to the approach of manufacturing the usable bulking agent for chromatographies to quantitive analysis by reduction of an unreacted silanol group, about the manufacturing method of the bulking agent for chromatographies which inactivates the residual silanol group of silica gel effectively.
[0002]
[Description of the Prior Art] In the existing bulking agent for high performance chromatography, the bulking agent which carried out the chemical bond of various kinds of organic silane compounds to silica gel is the general-purpose, and an octadecyl chlorosilicane compound, an octyl chlorosilicane compound, a butylchlorosilane compound, a cyano propyl chlorosilicane compound, a phenyl chlorosilicane compound, etc. exist as a typical organic silane compound. Among these, while the octadecyl silica gel bulking agent (ODS) is used most extensively, this bulking agent is on analysis and there are many advantages, there are also by no means few troubles of connoting.
[0003] Generally, the remarkable unreacted silanol group remains on the front face of silica gel whose above chemically bonded silica gel bulking agents are base materials. This unreacted silanol group is [0004] which was difficult to acquire the faithful repeatability of chromatogram by acting strongly with a polar substance, especially an alkali, adsorbing this alkali or causing the tailing phenomenon of a peak.
[Problem(s) to be Solved by the Invention] The following means exist as an approach of inactivating such a residual silanol group.
** Carry out the heating reflux of the chemically bonded silica gel bulking agent in solvents, such as toluene, with trimethylchlorosilane and a trimethylsilylation agent like hexamethyldisilazane.
** React the aforementioned ** under a high-pressure elevated temperature (Chromatograpy, Vol.17, 39, 1996).
** Make a chemically bonded silica gel bulking agent react at the temperature of 250 degrees C or more in a gaseous phase with an independent sililation reagent like hexamethyldisilazane, a trimethyl methoxy silane, and hexa methyl cyclotrisiloxane.
[0005] About the aforementioned ** and **, an unreacted silanol group still carries out considerable-amount survival of the bulking agent processed by these approaches. Moreover, by the approach of the aforementioned **, since the thermal desorption of the chemical modification radical by which the chemical bond was already carried out occurs while inactivation is improved considerably, there is a fundamental defect in which the property as a bulking agent changes.
[0006] this invention persons conducted much experiments while examining various the aforementioned problems in a chemically bonded silica gel bulking agent. When at least two sorts of end addition agents which form a complex compound were made to react with chemically bonded silica gel as the result, the residual silanol group found out that the fully inactivated bulking agent was compoundable irrespective of the inside of a gaseous phase or the liquid phase.

[0007] This invention is proposed in order to improve the trouble about the residual silanol group in a chemically bonded silica gel bulking agent, and it aims at offering the manufacturing method of the bulking agent for chromatographies which can inactivate the residual silanol group of this silica gel effectively in a gaseous phase or the liquid phase. Other purposes of this invention are offering the manufacturing method of the bulking agent for chromatographies which can be used for quantitative analysis by sufficient reduction of an unreacted silanol group.
[0008]
[Means for Solving the Problem] In order to attain the above-mentioned purpose, in the manufacturing method of the bulking agent for chromatographies concerning this invention, the chemical bond of the chemical modification agent is first carried out to the silanol group of silica gel. At least two sorts of end addition agents which form a complex compound in part at least are made to react with silica gel in a gaseous phase or the liquid phase after that. In this case, the conditions of a gaseous phase are heated at 180-240 degrees C in the well-closed container under an inert gas ambient atmosphere, and the conditions of the liquid phase are heated at 180-240 degrees C in the well-closed container under an inert gas ambient atmosphere.
[0009]
[Embodiment of the Invention] Although especially the silica gel used by this invention approach is not restricted, it is usually 10-500m2/g in the particle size of 1-1000 micrometers at 50-2000A and specific-surface-area of 1-1000m 2/g preferably [ it is desirable, is desirable at 3-100 micrometers and 10-5000A of pore size, and ].
[0010] By this invention approach, an organic silane compound well-known as a chemical modification agent can be used. For example, in chlorosilicane or alkoxysilane, they are 1 or two or more cyano groups in the aryl group of the carbon numbers 6-16, such as an alkyl group of the carbon numbers 1-30, such as a thoria KONCHIRU radical, a ray KOSHIRU radical, an octadecyl radical, an octyl radical, and n-butyl, and a phenyl group, or the alkyl group of carbon numbers 1-18, a hydroxyl group, a carboxyl group, an amino group, and an acid-amide radical as a chemical modification radical. As an alkoxy group of said alkoxysilane, the methoxy group, the ethoxy radical, etc. are suitable. Moreover, the cyclosiloxane and the polysiloxane which have the 2-8 aforementioned chemical modification radicals can also be used.
[0011] That is, what is necessary is for this chemical modification agent to be a monochloro silane compound, a dichlorosilane compound, a trichlorosilane compound, a mono-alkoxysilane compound, a dialkoxy silane compound, a trialkoxysilane compound, a cyclosiloxane compound, and a polysiloxane compound, and just to choose it from the inside of this at least one sort. As a concrete chemical modification agent Dimethyloctadecyl chlorosilicane, a dimethyloctadecyl methoxy silane, octadecyl trichlorosilane, octadecyltrimethoxysilane, dimethyl octyl chlorosilicane, octyl trichlorosilane, n-buthyldimethyl chlorosilicane, Di-n-butyl dichlorosilane, n-butyl-trichlorosilane, dimethylphenyl chlorosilicane, diphenyl dichlorosilane, phenyl trichlorosilane, 3-cyano propyl dimethyl chlorosilicane, 3-cyano propyl trichlorosilane, Hexa methyl cyclotrisiloxane etc. can be illustrated.
[0012] The reaction of silica gel and a chemical modification agent can be performed on a well-known approach and well-known conditions, and makes silica gel and a chemical modification agent react in a solvent generally. What is necessary is not to react with a chemical modification agent and just to use a stable solvent thermally under reaction temperature like toluene and a xylene, as this solvent. Reaction temperature is usually 30-350 degrees C, the range of reaction time is 24 hours from 30 minutes, and a reaction environment should just be a direct vent system under inert gas ambient atmospheres, such as an opening type or nitrogen.
[0013] Chemical modification silica gel and the end addition agent made to react consist of at least two sorts of reaction agents which form a complex compound, and the end addition agent of one of these is a silazane compound, a disilazane compound, a siloxane compound, or a polysiloxane compound. Moreover, the end addition agent of another side consists of a halogeno silane compound, an alkylcarbonyloxy silane compound, an alkylsulfonyloxy silane compound, an alkyl borane compound, a dialkylzinc compound, an alkylaluminum compound, an alkyl titanium compound, or an alkyltin compound. Each end addition agent may be mixed and used to one sort or three sorts.

[0014] Specifically, one end addition agents are N-(trimethylsilyl) morpholine, N-(trimethylsilyl) imidazole, hexamethyldisilazane, a trimethylsilyl acetamide, pentamethyldisiloxane, hexa methyl disiloxane, etc. Moreover, the end addition agent of another side is a trimethyl BUROMO silane, trimethylchlorosilane, a trimethyl iodine silane, trimethylsilyl acetate, trimethylsilyl trifluoroacetate, a trimethylsilyl trifluoromethane sulfonate, a trimethylsilyl methane sulfonate, triethylborane, diethyl methoxy borane, dimethyl zinc, diethylzinc, trimethylaluminum, triethylaluminum, a diethylaluminium chloride, titanium n-butoxide, or di-n-butyl-n-butoxy tin.
[0015] the approach of carrying out the chemical bond of the deactivating group to a residual silanol group -- chemical modification silica gel and at least two sorts of end addition agents -- a well-closed container -- putting in -- the bottom of inert gas ambient atmospheres, such as nitrogen, or reduced pressure -- the temperature of 180-240 degrees C -- it is 200-230 degrees C in temperature preferably, and is made to react from 1 hour preferably from 30 minutes in a gaseous phase for 24 hours for 48 hours Although the reaction in a gaseous phase is preferably performed under inert gas ambient atmospheres, such as nitrogen, an argon, and helium, it is also possible to carry out, where suction reduced pressure of the inside of the system of reaction is carried out with an aspirator etc. after a permutation with inert gas.
[0016] Although this chemical bond approach may be performed in the liquid phase, i.e., a solvent, it must be made to react in the well-closed container under an inert gas ambient atmosphere. In this case, what is necessary is just to use permutation aromatic compounds, such as aromatic hydrocarbon, such as toluene and a xylene, diphenyl ether, and o-dichlorobenzene, as a suitable solvent.
[0017] By this invention approach, when at least two sorts of end addition agents are mixed and a part of the mixture forms a complex compound, rather than a respectively independent end addition agent, trimethylsilylation of an unreacted silanol group is promoted much more effectively, and the chemical bond of the deactivating group is carried out to the residual silanol group of silica gel. Also in a gaseous phase, formation of this complex compound is possible also in the liquid phase, and can fully inactivate the residual silanol group of silica gel at low temperature comparatively in a well-closed container.
[0018] this invention approach does not almost have that reaction temperature can fully attain inactivation also at the low temperature of 180-240 degrees C, and the thermal desorption of the chemical modification radical which already carried out the chemical bond such by being a low-temperature reaction occurs. Therefore, more residual silanol groups of silica gel can be inactivated, and the defect in which the property as a bulking agent changes is not generated, either, rather than it adds an independent end addition agent.
[0019] As a preceding paragraph story of this invention approach, the example of manufacture which introduces a chemical modification radical to silica gel is indicated.
[0020] After carrying out the heating reflux of the porosity silica gel of example of manufacture 1 particle-size [ of 5 micrometers ], and 120A of pore size 50g in a dilute-hydrochloric-acid water solution, it carries out a ****** exception, and one by one, suction filtration of the solid which separated is carried out, and water and a methanol wash it. After suction reduced pressure furthermore removes a solvent, a silica gel particle is dried at 110 degrees C for 5 hours. 50g of dry silica gel particles is put into one liter flask, and desiccation toluene 500ml, dimethyloctadecyl chlorosilicane 46.9g (150m mol), and pyridine 15ml are added. After carrying out heating reflux for 6 hours, agitating this mixture, it cools to a room temperature and a solid is carried out a ****** exception. Suction filtration of this solid is carried out with toluene, 50% methanol, and a methanol one by one, it is washed, and silica gel 53g which carried out reduced pressure drying for 10 hours, and carried out dimethyloctadecyl silanizing at 60 degrees C next is obtained. The carbon content of this silica gel was 16.3% from elemental analysis.
[0021] 50g of silica gel particles which carried out dilute-hydrochloric-acid processing like the example 1 of example of manufacture 2 manufacture is put into a 1l. glass autoclave, and desiccation o-dichlorobenzene 350ml, dimethyloctadecyl chlorosilicane 46.9g (150m mol), and pyridine 15ml are added, and after carrying out the nitrogen purge of the inside of an autoclave, it seals. After heating at 180 degrees C for 8 hours, agitating this mixture, it cools to a room temperature and a solid is carried out a ****** exception. Washing and reduced pressure drying

of this solid are carried out like the example 1 of manufacture, and silica gel 52g which carried out dimethyloctadecyl silanizing is obtained. The carbon content of this silica gel was 16.5% from elemental analysis.

[0022] When the same actuation as the example 1 of manufacture is performed using the chemical modification agent 150m mol shown in the following table 1 instead of the dimethyloctadecyl chlorosilicane in the example 3 of manufacture – the example 1 of 12 manufactures, the chemical modification silica gel shown in Table 1 is obtained.

[0023]

[Table 1]

| 製造例番号 | 化学修飾剤 | 化学修飾したシリカゲル | |
|---|---|---|---|
| | | 収量（g） | 炭素含有率(%) |
| 3 | オクタデシルトリメトキシシラン | 54 | 16.1 |
| 4 | オクタデシルトリクロロシラン | 52 | 16.2 |
| 5 | ジメチルオクチルクロロシラン | 51 | 10.5 |
| 6 | オクチルトリクロロシラン | 49 | 10.2 |
| 7 | オクチルトリメトキシシラン | 50 | 10.1 |
| 8 | ジメチルブチルクロロシラン | 51 | 8.3 |
| 9 | ジブチルジクロロシラン | 49 | 10.0 |
| 10 | ジメチルフェニルクロロシラン | 52 | 9.8 |
| 11 | ジメチル3ーシアノプロピルクロロシラン | 49 | 7.8 |
| 12 | ジフェニルクロロシラン | 51 | 13.1 |

[0024]

[Example] Although this invention is explained based on an example, this invention is not limited to the following examples. In each example, the process which carries out the chemical bond of the deactivating group to the residual silanol group of chemical modification silica gel is indicated.

[0025] Silica gel 10g which was obtained in the example 1 of example 1 manufacture and which carried out dimethyloctadecyl silanizing, hexa methyl disiloxane 1.62g (10m mol), and trimethyl iodine silane 2.0g (10m mol) are put into a glass well-closed container (50 cc), and it decompresses and seals, after carrying out the nitrogen purge of the inside of this container. after heating 220 degrees C of this container in a thermostat for 8 hours -- cooling radiationally -- contents -- toluene 200ml -- suction filtration is carried out after making it suspend in inside. (Bulking agent I) 9.8g which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.

[0026] Silica gel 50g which was obtained in the example 2 of example 2 manufacture and which carried out dimethyloctadecyl silanizing, N-(trimethylsilyl) imidazole 7.0g (50m mol), and trimethylchlorosilane 5.4g (50m mol) are put into a glass well-closed container (300 cc), and it decompresses and seals, after carrying out the nitrogen purge of the inside of this container. after heating 230 degrees C of this container in a thermostat for 8 hours -- cooling radiationally -- contents -- toluene 500ml -- suction filtration is carried out after making it suspend in inside. Bulking agent (II)47.5g which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.

[0027] A dimethyl OKUDADESHIRU methoxy silane is used instead of the dimethyloctadecyl chlorosilicane in the example 1 of example 3 manufacture, and the silica gel which carried out dimethyloctadecyl silanizing by the same actuation as the example 1 of manufacture is obtained. This silica gel 50g, trimethylsilyl acetamide 6.6g (50m mol), and triethylborane 4.9g (50m mol) are added to diphenyl ether 250ml, and this is put into a glass well-closed container (500 cc), and it seals, after carrying out the nitrogen purge of the inside of this container. Agitating the inside of this container, it cools radiationally, after heating this container at 210 degrees C for 8 hours, and suction filtration of the contents is carried out. 48.5g (III) of bulking agents which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.

[0028] Silica gel 10g which was obtained in the example 4 - the example 1 of 10 manufactures and which carried out dimethyloctadecyl silanizing, and 10m each mol of mixture of the end addition agent shown in the following table 2 are put into a glass well-closed container (50 cc), and it decompresses and seals, after carrying out the nitrogen purge of the inside of this container. after carrying out time amount heating with temperature as shows this container in Table 2 in a thermostat -- cooling radiationally -- contents -- toluene 200ml -- suction filtration is carried out after making it suspend in inside. The bulking agent (IV-X) which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.

[0029]

[Table 2]

| 実施例番号 | 末端付加剤（少なくとも２種の混合） | 反応温度 反応時間 | 充填剤名 収量(g) |
|---|---|---|---|
| 4 | ヘキサメチルジシラザン | ２００℃ | (IV) |
| | トリメチルブロモシラン | １２hr | ９．２ｇ |
| 5 | Ｎ－（トリメチルシリル）モルホリン | ２１０℃ | (V) |
| | トリメチルシリルメタンスルホナート | ８hr | ９．０ｇ |
| 6 | ヘキサメチルジシラザン | ２３０℃ | (VI) |
| | トリメチルシリルトリフルオロアセテート | ８hr | ９．２ｇ |
| 7 | ヘキサメチルジシラザン | ２２０℃ | (VII) |
| | トリメチルクロロシラン | ８hr | ９．５ｇ |
| 8 | ヘキサメチルジシラザン | １９５℃ | (VIII) |
| | ジメチルブロモシラン | １８hr | ９．３ｇ |
| | トリエチルボラン | | |
| 9 | ヘキサメチルジシラザン | １８０℃ | (IX) |
| | トリメチルブロモシラン | １８hr | ９．６ｇ |
| １０ | ヘキサメチルジシラザン | ２４０℃ | (X) |
| | ジ－ｎ－ブチル－ｎ－ブトキシスズ | ８hr | ９．５ｇ |

[0030] Silica gel 10g which was obtained in the example 11 - the example 1 of 17 manufactures and which carried out dimethyloctadecyl silanizing, and 10m each mol of mixture of the end addition agent shown in the following table 3 are put into a glass well-closed container (50 cc), and it seals, after carrying out the nitrogen purge of the inside of this container. after carrying out time amount heating with temperature as shows this container in Table 3 in a thermostat -- cooling radiationally -- contents -- toluene 200ml -- suction filtration is carried out after making it suspend in inside. The bulking agent (XI-XVII) which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene,

methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.
[0031]
[Table 3]

| 実施例番号 | 末端付加剤（少なくとも２種の混合） | 反応温度 反応時間 | 充填剤名 収量(g) |
|---|---|---|---|
| １１ | ヘキサメチルジシロキサン | ２１０℃ | (XI) |
| | トリメチルブロモシラン | 8hr | 9.0g |
| １２ | ヘキサメチルジシラザン | ２２５℃ | (XII) |
| | ジエチルメトキシボラン | 8hr | 9.6g |
| １３ | ヘキサメチルジシラザン | ２１０℃ | (XIII) |
| | トリメチルクロロシラン | 8hr | 9.2g |
| １４ | ヘキサメチルジシラザン | ２００℃ | (XIV) |
| | トリメチルシリルトリフルオロアセテート | 9hr | 9.5g |
| １５ | ヘキサメチルジシラザン | １９５℃ | (XV) |
| | トリメチルクロロシラン | １５hr | 9.0g |
| | トリエチルボラン | | |
| １６ | ヘキサメチルジシラザン | ２３０℃ | (XVI) |
| | ジ－ｎ－ブチル－ｎ－ブトキシスズ | 8hr | 9.6g |
| １７ | Ｎ－（トリメチルシリル）イミダゾール | ２１０℃ | (XVII) |
| | トリメチルブロモシラン | １２hr | 9.2g |

[0032] The solvent shown in 10m each the mol and Table 4 of mixture of the end addition agent shown with silica gel 10g which was obtained in the example 18 - the example 1 of 24 manufactures, and which carried out dimethyloctadecyl silanizing in the following table 4 is put into a glass well-closed container (50 cc), and it seals, after carrying out the nitrogen purge of the inside of this container. Agitating the inside of this container, it cools radiationally, after carrying out time amount heating with temperature as shows this container in Table 4, and suction filtration of the contents is carried out. The bulking agent (XVIII-XXIV) which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water (1:1), and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.
[0033]
[Table 4]

| 実施例番号 | 末端付加剤（少なくとも２種の混合） | 溶媒 | 反応温度 反応時間 | 充填剤名 収量(g) |
|---|---|---|---|---|
| １８ | ヘキサメチルジシロキサン トリメチルブロモシラン トリエチルボラン | ｏ－ジクロロベンゼン | ２１０℃ １６hr | (XVIII) ９．０ｇ |
| １９ | ヘキサメチルジシラザン トリメチルブロモシラン | 〃 | ２２０℃ １６hr | (XIX) ９．６ｇ |
| ２０ | ヘキサメチルジシラザン トリメチルクロロシラン | 〃 | ２３０℃ １０hr | (XX) ９．４ｇ |
| ２１ | ヘキサメチルジシラザン トリメチルシリルトリフルオロアセテート | 〃 | ２１５℃ １５hr | (XXI) ９．６ｇ |
| ２２ | ヘキサメチルジシラザン ジ－ｎ－ブチル－ｎ－ブトキシスズ | ジフェニルエーテル | ２４０℃ １０hr | (XXII) ９．３ｇ |
| ２３ | ヘキサメチルジシラザン トリメチルクロロシラン ジエチルメトキシボラン | 〃 | ２２５℃ ８hr | (XXIII) ９．０ｇ |
| ２４ | トリメチルシリルアセトアミド トリメチルブロモシラン | 〃 | ２１５℃ １５hr | (XXIV) ９．８ｇ |

[0034] Example of a trial Change in carbon content and elemental analysis of the bulking agent which introduced the deactivating group in the pyridine-phenol analysis examples 1-24 are performed. Moreover, in order to obtain the chromatogram of the pyridine phenol analysis by these bulking agents, the column made from stainless steel with a bore [ of 4.6mm ] and a die length of 150mm is filled up with each bulking agent, and 7micro (each content is 0.07microl. [ ml ] /and 0.8mg/ml) of mixed samples I of a pyridine and a phenol is poured in as a mobile phase on acetonitrile/water (volume ratios 30/70), and 1ml a part for /and temperature of 37 degrees C of the rates of flow, and the detection wavelength of 254nm.

[0035] The obtained chromatogram is illustrated from drawing 1 to drawing 3 . The bulking agent which obtained drawing 1 in the example 1, the bulking agent which obtained drawing 2 in the example 7, and drawing 3 are the chromatograms by the bulking agent obtained in the example 16, and it experiments about other bulking agents. From the obtained chromatogram, the tailing factor of a pyridine, the degree of separation Rs of a phenol, and a pyridine is computed, and these results are summarized in the following table 5.

[0036] In here, the value of degree of separation Rs and a tailing factor is defined like following several 1 and several 2.

[0037]

[Equation 1]

$$\text{分離度 Rs} = 1.18 \times \frac{t_{R2}\ (\text{フェノール}) - t_{R1}\ (\text{ピリジン})}{W_{h/2}\ (\text{フェノール}) + W_{h/2}\ (\text{ピリジン})}$$

Peak width [ in / among a formula tR, and / in Wh/2 / one half of the height of a peak height ] is shown from the peak baseline of each compound. [ the holding time (minute) of each compound ]

[0038]

[Equation 2]

$$\text{テーリングファクター} = \frac{W_{h/20}}{2a}$$

Peak width [ in / in Wh/20 / 1/20 of the height of a peak baseline to a peak height ] and a show the distance of the perpendicular from peak top-most vertices, the supporting point of Wh/20, and the standup point of a peak in Wh/20 among a formula.

[0039]

[Table 5]

| 充填剤番号 | 元素分析 | | ピリジン-フェノール分析 | |
|---|---|---|---|---|
| | 炭素含有量(%) | その増減(%) | 分離度Rs | テーリングファクター |
| I | 16.4 | +0.6 | 15.7 | 1.27 |
| II | 16.5 | 0 | 15.9 | 1.24 |
| III | 16.4 | +0.6 | 16.7 | 1.18 |
| IV | 16.5 | +1.2 | 17.0 | 1.10 |
| V | 16.3 | 0 | 17.2 | 1.11 |
| VI | 16.1 | −1.2 | 15.6 | 1.25 |
| VII | 16.5 | +1.2 | 16.9 | 1.09 |
| VIII | 16.3 | 0 | 17.0 | 0.93 |
| IX | 16.5 | +1.2 | 16.6 | 1.15 |
| X | 15.9 | −2.5 | 15.4 | 1.29 |
| XI | 16.4 | +0.6 | 17.2 | 1.10 |
| XII | 16.8 | +3.1 | 16.8 | 1.15 |
| XIII | 16.6 | +1.8 | 17.1 | 1.08 |
| XIV | 16.4 | +0.6 | 17.2 | 1.08 |
| XV | 16.2 | −0.6 | 15.7 | 1.28 |
| XVI | 16.1 | −1.2 | 15.3 | 1.32 |
| XVII | 16.3 | 0 | 16.5 | 1.20 |
| XVIII | 16.6 | +1.8 | 17.2 | 1.11 |
| XIX | 16.4 | +0.6 | 17.3 | 1.07 |
| XX | 16.7 | +2.5 | 16.2 | 1.19 |
| XXI | 16.6 | +1.8 | 17.1 | 1.05 |
| XXII | 16.5 | +1.2 | 17.3 | 1.03 |
| XXIII | 16.7 | +2.5 | 16.1 | 1.20 |
| XXIV | 16.6 | +1.8 | 16.8 | 1.13 |

[0040] If the result of the elemental analysis of Table 5 is examined, reduction in a carbon content will be looked at by only bulking agents VI, X, XV, and XVI, and the carbon content will not decrease in the other bulking agent. Consequently, it is admitted that there is little thermal desorption of a chemical modification radical (this trial is a dimethyloctadecyl radical), and it becomes clear that this invention approach is excellent especially as a method of inactivating an end group.

[0041] Moreover, from the result of pyridine-phenol analysis, the degree-of-separation Rs values of a pyridine/phenol are 15.3-17.3, and it can judge with the silanol group of the bulking agent in Table 5 being inactivated nearly completely compared with the Rs values 8-14 of the column of the commercial same type. This reason is because the holding time of an alkali pyridine becomes

short and the degree of separation Rs with a phenol become large, so that there are few residual silanol groups. Furthermore, this reason is affirmable also from the value of the tailing factor of a pyridine. In the bulking agent in Table 5, the tailing factor values of a pyridine are 0.93-1.32, and it turns out in the column of the commercial same type that inactivation is progressing compared with 1.5 or more being common.

[0042] Silica gel 10g each which was obtained in an example 25 - the examples 3-12 of 34 manufactures and which was chemical-modification-ized, and 10m each mol of mixture of the end addition agent shown in the following table 6 are put into a glass well-closed container, and it decompresses and seals, after carrying out the nitrogen purge of the inside of this container. after carrying out time amount heating with temperature as shows this container in Table 6 in a thermostat -- cooling radiationally -- contents -- toluene 200ml -- suction filtration is carried out after making it suspend in inside. The bulking agent (XXV-XXXIV) which introduced the deactivating group is obtained by carrying out suction desiccation, after carrying out washing filtration with toluene, methanol-water, and a methanol further one by one, and carrying out reduced pressure drying at 60 more degrees C for 10 hours.

[0043]

[Table 6]

| 実施例番号 | 化学修飾したシリカゲル | 末端付加剤（少なくとも2種の混合） | 反応温度 反応時間 | 充填剤名 収量(g) |
|---|---|---|---|---|
| 25 | 製造例3 | ヘキサメチルジシロキサン<br>トリメチルヨードシラン | 220℃<br>8hr | (XXV)<br>9.5g |
| 26 | 製造例4 | N-（トリメチルシリル）<br>イミダゾール<br>トリメチルクロロシラン | 220℃<br>10hr | (XXVI)<br>9.7g |
| 27 | 製造例5 | ヘキサメチルジシラザン<br>トリメチルクロロシラン | 200℃<br>12hr | (XXVII)<br>9.1g |
| 28 | 製造例6 | ヘキサメチルジシラザン<br>トリメチルシリルトリフルオロアセテート | 220℃<br>10hr | (XXVIII)<br>9.4g |
| 29 | 製造例7 | ヘキサメチルジシラザン<br>トリメチルブロモシラン | 210℃<br>12hr | (XXIX)<br>9.3g |
| 30 | 製造例8 | ヘキサメチルジシラザン<br>トリメチルクロロシラン | 210℃<br>10hr | (XXX)<br>9.4g |
| 31 | 製造例9 | ヘキサメチルジシロキサン<br>トリメチルブロモシラン | 210℃<br>14hr | (XXXI)<br>9.2g |
| 32 | 製造例10 | ヘキサメチルジシラザン<br>トリメチルシリルトリフルオロアセテート | 205℃<br>10hr | (XXXII)<br>9.5g |
| 33 | 製造例11 | ヘキサメチルジシラザン<br>トリメチルクロロシラン | 210℃<br>12hr | (XXXIII)<br>9.1g |
| 34 | 製造例12 | ヘキサメチルジシロキサン<br>トリメチルブロモシラン | 215℃<br>10hr | (XXXIV)<br>9.3g |

[0044]

[Effect of the Invention] By this invention approach, at least two sorts of end addition agents are mixed, and when a part of the mixture forms a complex compound, inactivation of an unreacted silanol group is promoted further. When reaction temperature attains effective inactivation also at the low temperature of 180-240 degrees C, the thermal desorption of the chemical

modification radical which already carried out the chemical bond does not generate this invention approach. Therefore, if this invention is used, the defect in which the property as a bulking agent changes like before in the case of inactivation of a residual silanol group does not occur, but the bulking agent with which the residual silanol group was fully inactivated can be compounded irrespective of the inside of a gaseous phase or the liquid phase.

[0045] The unreacted silanol group in the front face of the silica gel which is a base material almost disappears, and causing the tailing phenomenon of adsorption of an alkali or a peak by the unreacted silanol group cancels the silica gel bulking agent manufactured by this invention approach. The advantage on the analysis in the conventional chemical bond mold bulking agent is held, and also this silica gel bulking agent can acquire the faithful repeatability of chromatogram.

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[Translation done.]

* NOTICES *



1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

## DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] It is the chromatogram of the pyridine phenol analysis by the bulking agent obtained in the example 1.
[Drawing 2] It is the chromatogram of the pyridine phenol analysis by the bulking agent obtained in the example 7.
[Drawing 3] It is the chromatogram of the pyridine phenol analysis by the bulking agent obtained in the example 16.

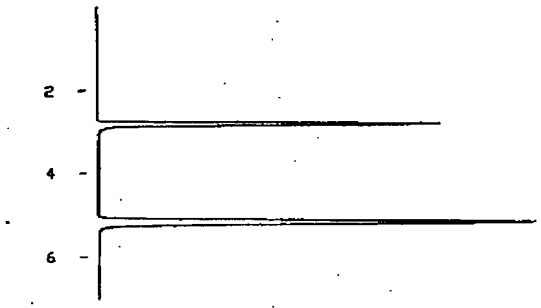
[Translation done.]

* NOTICES *

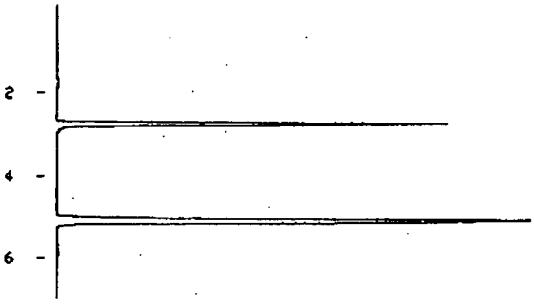


DRAWINGS

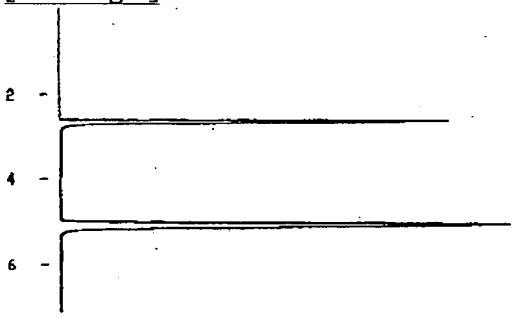
[Drawing 1]




[Drawing 2]




[Drawing 3]




[Translation done.]